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Section: Original Research

Article Title: Substituting Sedentary Time With Light And Moderate-to-Vigorous Physical Activity is Associated With Better Cardio-Metabolic Health

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Abstract

Background: Apply a more novel approach to systematically examine (1) associations of clustered cardio-metabolic risk and cardio-metabolic risk factors, and (2) theoretical substitution of sedentary time with either sleep, light physical activity (LPA) or moderate-and-vigorous physical activity (MVPA) and substituting LPA with MVPA. **Methods:** Physical activity and sleep were objectively measured in 410 Flemish adults (55.5[±9.6] years, 64% men) with a SenseWear Pro 3 Armband. Cardio-metabolic risk factors (obesity, hyperglycemia, dyslipidemia, and hypertension,), cardiorespiratory fitness were objectively measured. Isotemporal substitution analyses were performed to assess the associations between substituting time from a potentially negative behavior into another, potentially positive, behavior. **Results:** Theoretical substitution of sedentary time with MVPA was associated with decreased clustered cardio-metabolic risk (b = -0.06 [-0.08;-0.04]) and substituting LPA with MVPA was associated with a decrease in clustered cardio-metabolic risk (b = -0.08 [-0.11;-0.04]). Substituting sedentary time with LPA or sleep improved HDL-cholesterol, systolic and diastolic blood pressures, and waist circumference. **Conclusion:** Theoretical replacement of sedentary time with either sleep, LPA or MVPA was positively associated with improved cardio-metabolic risk factor status. Interventions for increasing cardio-metabolic health can focus on replacing sedentary time with either sleep, LPA or MVPA depending on the risk parameters that need to be targeted.

Background

The cardio-metabolic health benefits of physical activity can no longer be denied, as the lack of physical activity is one of the most important predictors of mortality and burden of disease [1]. Lately, sedentary time has also been confirmed as a cardio-metabolic health risk in itself, and meeting the guidelines for physical activity does not make up for a sedentary lifestyle [2]. Therefore, it is important to accumulate 150 minutes of moderate-intensity physical activity a week and try to limit prolonged sedentary time during waking hours [3-5]. However, as our day is limited to 24h, the question arises as to what changes in health will result from substituting a potentially negative behavior with a potentially positive behavior. Furthermore, sleep has also been suggested as an important predictor for cardio-metabolic health, where short and long sleep durations are associated with an increased risk for cardio-metabolic diseases [6].

Recently, a relatively new method of analysis, isotemporal substitution, was introduced. This technique estimates the effect of replacing one form of behavior with another form of behavior for the same amount of time [7]. An important benefit is that it not only estimates the effect of increasing a certain behavior, but also integrates the effect of reducing the specific behavior that it replaced [7]. For example, reducing sedentary time and replacing it with sleep or light-intensity physical activities (LPA) may result in a different health benefit than replacing the same amount of sedentary time with moderate-to-vigorous physical activity (MVPA) [8-11]. Results from previous research clearly state that substituting sedentary time with MVPA will lead to lower clustered cardio-metabolic health risk, than substituting with LPA or sleep. Nonetheless, some uncertainty remains whether substituting sedentary time with LPA will already have positive results; or whether only substitution with higher intensities such as MVPA have beneficial results [8-10,12]. Furthermore, only a few authors included substituting sedentary time with sleeping time, and sleeping time with physically-active behaviors, such as LPA or MVPA [8,13]. These data demonstrated that substituting sedentary time with sleep reduced clustered cardio-metabolic risk [8], but potentially only in low sleepers (i.e. sleeping ≤ 7 h/day) [13]. However, none of these studies included objectively measured sleeping time.

Therefore, the purpose of the current study was to apply a novel approach to systematically examine the cardio-metabolic health benefits of substituting sedentary time with either sleep, LPA or MVPA. Furthermore, the extra benefit of increasing physical activity intensity from LPA to MVPA, was also explored. Firstly, we hypothesized that substituting sedentary time with either sleep, LPA or MVPA, would be associated with a lower clustered cardio-metabolic risk and better outcomes on five cardio-metabolic health factors (waist circumference, fasting glucose, triglycerides, High Density Lipoprotein cholesterol (HDL-cholesterol), and blood pressure). Secondly, we hypothesized that substituting LPA with MVPA would be associated with a small, but significantly reduced clustered cardio-metabolic risk and its factors.

Methods

Subjects and study design

Data for the present study were collected by the Flemish Policy Research Centre Sport between 2012 and 2014, in a cross-sectional survey on the relationship among physical activity, physical fitness and several health parameters. Participants were randomly recruited by the National Institute for Statistics or as part of a study running since 1969 at the KU Leuven [14], which resulted in male (n = 420) and female (n = 232) volunteers between 29 and 82 years. Due to rigorous measurement methods and strict inclusion criteria not all participants were included in the final sample. For 445 participants valid physical activity data were available. Some participants had missing values for cardio-metabolic markers or covariates, leaving a final sample of 410 (63%). An informed consent was obtained from the participants and the study was approved by the Medical Ethics Committee of the KU Leuven (s54083).

Physical activity, sedentary behavior and sleep

Objective measurement of physical activity was obtained with a multi-sensor SenseWear Pro 3 Armband® (BodyMedia, Inc, Pittsburgh, PA, USA), which generates valid results for daily energy expenditure under free-living conditions [15-17]. Estimates of sleep and wake parameters were extracted from multiple sensors (i.e. two-axis accelerometer, heat flux sensor, galvanic skin response sensor, skin temperature sensor, and near body ambient temperature sensor) and were combined with sex, age, body mass, and height, using proprietary algorithms developed by the manufacturer (SenseWear Professional software, version 6.1). Participants were asked to wear the monitor for seven consecutive days, 24 hours a day, except during water-based activities. The compliance criterion was set at 1296 minutes (90%) a day. This threshold corresponds with the more often used 600 min/day threshold for accelerometer-based monitors that are worn during waking hours only [18,19]. Furthermore, to achieve reliable estimates of total physical activity, only subjects who met the compliance criterion of at least 3 weekdays and both weekend days were admitted, resulting in the exclusion of 207 (32%) of the original 652 participants [20]. A drop-out analyses between people complying to the acceptation criteria and not-complying, was performed to examine if not-complying to the guidelines was random. The following physical activity intensity categories were assigned to wake time: Sedentary time <=1.5 MET, LPA 1.5 – 3 MET; and MVPA as >3 MET, sleep time was defined by algorithms developed by the manufacturer [17].

Cardio-metabolic risk factors and a clustered cardio-metabolic risk score

A clustered cardio-metabolic risk score (CMRS) was calculated to asses cardio-metabolic risk on a continuous manner [21]. Metabolic factors were assessed by trained staff in the morning after an overnight fast. Waist circumference was measured between the lower rib and the iliac crest to the nearest 0.1 cm. Following five minutes of rest, systolic and diastolic blood pressures were measured three times using an electronic monitor (Omron, The Netherlands) in seated position from the right arm. The means of the three measurements were used in statistical analyses. Triglycerides, plasma glucose, and HDL-cholesterol were obtained from an antecubital vein and analyzed by enzymatic methods (Abbott Laboratories, Abbott Park, IL). Due to skewness, values for the latter three risk factors were first normalized ($\log_{10}$). Subsequently, each cardio-metabolic variable was standardized using Z-scores by using the sex-specific baseline sample mean and standard deviation, derived from all men and women with baseline data for each cardio-metabolic variable. To calculate the CMRS, the sum of these standardized values was divided by the number of metabolic factors included (n = 5).

Covariates

Smoking behavior was assessed using the WHO Monica Smoking Questionnaire [22]. Participants were classified as current, former or never smokers. Education level was used as an indicator of socio-economic status, and was ranked in four categories, ranging from no degree or primary school degree; secondary school degree; professional bachelor degree; and higher.

Nutritional intake was assessed using a three-day diet record, during two weekdays and one weekend day. Participants were instructed to weigh and record all foods and drinks or estimate portions using standard household measures such as a plate, spoon or glass. From these records, an overall diet quality indicator, the Healthy Eating Index (HEI), was calculated using Becel Nutrition software (Unilever Co., Rotterdam, The Netherlands)[23]. The HEI is scored on a scale from 0 to 100 and was included as a descriptive variable.

Peak VO_2 was determined by means of a maximal exercise test on an electrically braked Lode Excalibur cycle ergometer® (Lode, Groningen, The Netherlands). Oxygen consumption was measured directly using breath-by-breath respiratory gas exchange analysis, using a Cortex MetaLyzer 3B analyzer (Cortex Biophysic GmbH, Leipzig, Germany) [24]. Participants were verbally encouraged to reach a maximal level of volatile exertion and the test was terminated when subjects were exhausted or when the physician stopped the test for medical reasons. Participants first had to pass a physical examination and people at risk for heart failure and arterial hypertension did not participate in the maximal exercise test.

Statistical analysis

Descriptive statistics (means and standard deviations) were calculated for all variables and presented for the entire sample. The association between sleep and CMRS was tested for linearity to determine whether analyses needed to be corrected for sleep duration. Pearson correlations were calculated to determine associations between sleep and various physical activity intensities and cardio-metabolic health.

The isotemporal substitution model, by definition, estimates the effect of replacing one physical activity type with another physical activity type for the same amount of time [7]. An isotemporal substitution analysis (Model 1) was presented to examine the associations between replacing sedentary time with an equivalent time of sleep, LPA or MVPA, and cardio-metabolic health.

Isotemporal substitution requires approximately linear associations between each exposure and the outcome, therefore linearity was tested together with all other relevant assumptions. All non-standardized activity variables (sleep, LPA, MVPA), with the exception of sedentary time, were simultaneously included into a regression model, along with a total wear time variable and all relevant covariates (age, sex, education level, HEI and smoking status). The total wear time variable represents the time of the omitted activity and therefore total time is constant [7]. Substitution model 1 is expressed as follows:

Cardio-metabolic risk = *(b1)* sleep + *(b2)* LPA + *(b3)* MVPA + *(b4)* total wear time + *(b5)* covariates.

The remaining *b1*, *b2*, *b3*-coefficients can be interpreted as follows: They represent the increase or decrease in cardio-metabolic health by substituting that activity instead of sedentary time, while holding other activity types constant.

Similarly, a model was constructed with sleep, sedentary time, MVPA, covariates and total wear time, leaving out LPA (Model 2).

Cardio-metabolic risk = *(b1)* sleep + *(b2)* sedentary time + *(b3)* MVPA+ *(b4)* total wear time + *(b5)* covariates.

All statistical analyses were performed using the SAS statistical program, version 9.4 (SAS institute, Cary, NC, USA). Statistical significance was set at $p < .05$ and all statistical tests were two-tailed.

Results

Analyses included 410 subjects, 64% men with a mean age of 55.5 (±9.6) years. The majority of the population had a higher education (58%) and had never smoked (56%) or were former smokers (36%), and had an average HEI of 49 (±10). Table 1 presents the descriptive statistics of the participants for personal characteristics, sleep, physical activity, and cardio-metabolic markers. Total wear time was 1,424 (±12) minutes, which is 99% of a day. The average VO_2peak of the participants (n=328) was 33.8 (±9.1) $ml.min^{-1}.kg^{-1}$.

Only two participants slept more than nine hours a day, but 120 (29%) participants had a short sleep duration of less than six hours, including 30 (7%) participants sleeping less than five hours a day. The association between sleep and CMRS was linear and there were no significant differences in cardio-metabolic parameters and MVPA between short and normal sleep durations (results not shown). Therefore, analyses were not stratified by sleep duration.

Sedentary time was correlated with sleep (r = -0.40, $p < .001$), LPA (r = -0.42, $p < .001$) and MVPA (r = -0.62, $p < .001$). Sleep was correlated with LPA (r = -0.12, $p < .05$) and LPA with MVPA (r = -0.21, $p < .001$). MVPA and sleep were not significantly correlated. No multicollinearity between activity variables was present considering a cut-off of 0.7. Pearson correlation coefficients for the association between sleep, sedentary time, and physical activity; and cardio-metabolic risk factors are presented in Table 2.

Unstandardized regression coefficients and 95% confidence intervals of substituting sedentary time with sleep, LPA or MVPA are reported in Table 3. Substituting sedentary time with sleep was associated with a significant decrease in waist circumference. Substituting sedentary time with sleep or LPA was not associated with clustered cardio-metabolic risk. However, substituting sedentary time with LPA was associated with an increased HDL-cholesterol; and lower waist circumference, and both systolic and diastolic blood pressures. Lastly, substituting sedentary time with MVPA was associated with a significantly lower clustered cardio-metabolic risk, waist circumference, and triglycerides; and higher HDL-cholesterol. Unstandardized regression coefficients can be small, because these coefficients represent absolute changes in health and the standard units for some of the health parameters are rather small.

Similarly, regression coefficients and 95% confidence intervals of substituting LPA with sleep, sedentary time and MVPA are presented in Table 4. Substituting LPA with sleep was not associated with changes in clustered cardio-metabolic risk and its factors. However, substituting LPA with sedentary time was associated with an increase in waist circumference, and both systolic and diastolic blood pressures; and a decrease in HDL-cholesterol. Furthermore, substituting LPA with MVPA was associated with a decrease in clustered cardio-metabolic risk, a decrease in HDL-cholesterol, and an increase in diastolic blood pressure.

Discussion

The primary finding of this study is that a substitution of sedentary time with either sleep, LPA or MVPA was associated with several health improvements. Findings suggest that substituting sedentary time with LPA can improve various cardio-metabolic risk factors such as waist circumference, HDL-cholesterol, and systolic and diastolic blood pressures. However, a substitution of sedentary time with MVPA, was only significantly associated with a decrease in clustered cardio-metabolic risk. Furthermore, analyses for substituting LPA with MVPA were executed to explore the extra benefit of substituting LPA with higher intensities of physical activity. Again, a significant association was present for clustered cardio-metabolic risk, but increasing exercise intensity did not lead to a further gain for other cardio-metabolic parameters. Contrary, substituting LPA with MVPA was associated with a small decrease in HDL-cholesterol and an increase in diastolic blood pressure. We have no direct explanation for these contradictory results. Biological plausible reasons for improved health with higher levels of physical activity are hypothesized to act through beneficial changes in fibrinolytic, hemodynamic and inflammatory markers, blood pressure, and the cardiovascular system [25]. However, the mechanisms that underline the associations between sleep and health are not fully understood [6]. An investigation reporting an association between sleep duration and variants of the human Circadian Locomotor Output Cycles Kaput (CLOCK) genes suggested that disruptions of the core CLOCK genes, which regulate endogenous circadian rhythmicity, are linked to perturbations in glucose metabolism, adipocyte and vascular function, and obesity [26].

Results are in line with previous research applying isotemporal substitution to explore the association between sedentary time, physical activity, and clustered cardio-metabolic risk [8-10]. All previous studies observed beneficial effects of substituting sedentary time with MVPA for clustered cardio-metabolic risk and several of its parameters [8,9], starting from as little as one minute [10]. However, where some studies also found clustered cardio-metabolic risk improvements for substituting sedentary time with LPA [8,10], our study did not observe a significant association. Nevertheless, this is in line with the study by Hamer et al., who argued that the association of sedentary time and clustered cardio-metabolic risk may be dependent on the type of activity that will displace sedentary time [9]. Then again, our results suggest that for some cardio-metabolic health parameters substituting sedentary time with LPA can lead to positive effects. Therefore, not only the type of activity that displaces sedentary time is important, but also the health parameter in question, where substitution with LPA might be valuable for waist circumference, HDL-cholesterol, and both systolic and diastolic blood pressures.

Because a significant trend was observed in the number of risk factors with a decline in VO_2peak, all analyses were further adjusted for cardiorespiratory fitness. However, results and effect sizes were of similar proportion. One other study including isotemporal substitution performed additional analyses adjusting for estimated VO_{2max} and also found no significant change in point estimates [10]. Another study examining markers of glucose regulation explored the effects in high and low fit participants and suggested that low fit participants might benefit more from replacing sedentary time with active behavior [12].

The dose-response curve between physical activity and various health outcomes is a possible reason for the effect that results from substituting sedentary time or LPA with MVPA (i.e. greater increases in physical activity will lead to greater increases in health outcomes) [29]. This implies that greater health benefits can be reached by increasing the intensity of our behavior. Therefore, replacing a less intense behavior, such as sedentary time or LPA with a more intense behavior, such as MVPA, may lead to decreased cardio-metabolic risk. Furthermore, prolonged uninterrupted periods of sedentary time are associated with lower cardio-metabolic health [5]. By reducing sedentary time and introducing more active behavior, these prolonged periods of sedentary time will likely decrease and this will in turn have positive cardio-metabolic health effects [5,30].

To the best of our knowledge this is the first paper to include objective measurement of sleep when substituting sleep with sedentary time. In contrast to previous studies, we did not observe a U-shape relation between sleep duration and cardio-metabolic health [6]. This could possibly be explained by the low variability in sleep levels of our sample, with 93% of our participants sleeping between 5 and 9 hours a day. Additionally, no significant differences in cardio-metabolic health parameters were noted between participants with short and normal sleep duration. Therefore, unlike other studies [8,13], analyses for sleep were not preformed separately for long and short sleep durations and sleep was not treated as a piecewise variable. However, results were similar between all three studies indicating that replacing sedentary time with sleep can have positive effects on several cardio-metabolic health parameters [8,13].

Isotemporal substitution analyses assume a substitution of equal absolute bouts of time, however, substituting a certain bout of MVPA is a greater relative proportion of the baseline value, in comparison to the same bout of sedentary behavior or sleep. For example, the substitution of 30 minutes of sedentary time will only decrease the total average sedentary time with less than 5%, while adding 30 minutes of MVPA means an increase of 20% of the baseline MVPA. It is likely that because of these relative differences, substituting LPA by MVPA appears to have greater benefits than substituting sedentary time by MVPA (Tables 3 & 4).

Because, only 5% of a potentially harmful behavior (sedentary time) is changed, while 13% of LPA is changed into MVPA, possibly explaining the association with better cardiometabolic health.

Strengths of this study include the objective measurement of physical activity and sleep with a Sensewear Pro 3 and high inclusion criteria. Average wear time was 99% of a full day (minimum 5 days) and, as a consequence, all activities of daily living, excluding water based activities, were measured objectively. Moreover, all participants wore the Sensewear on both weekend days, and at least three weekdays to generate the most complete view of their activity behavior [20]. The Sensewear is valid for accurate measurement of daily energy expenditure under free-living conditions, with the exception of higher levels of expenditure [15]. However, only a small percentage of the activities were performed at such a high intensity level (5.8 [±9.1] minutes of vigorous physical activity a day) and few participants reached these high intensities. Contrary to most studies, the amount of MVPA in the current study was high, however, these levels of MVPA were similar to the levels found in a study on a comparable Flemish population [31], which might also be due to the specific algorithms of the SenseWear Pro 3. Furthermore, our recording of MVPA and sedentary time in single minutes instead of longer bouts (e.g. bouts of 10 min) might have resulted in a more inclusive measurement of MVPA. Alternatively, our study sample may have included healthier, more active, and more highly educated individuals compared to the average population.

Another strength is the use of isotemporal substitution analyses, because there are only 24h a day, adding one activity will certainly lead to reducing another activity. Consequently, the effect of increased time spent in a certain behavior, such as MVPA, might lead to different health effects when reducing different behaviors, such as sleep, LPA or sedentary behavior [7]. Furthermore, we included a population with a wide age-span to increase external validity. A potential downside of this wide age-span is that not all results are valid for every age, however, we performed age-specific analyses and observed no significant differences between age-groups. Finally, CRF was measured by a maximal cycle ergometer exercise test, generally considered the gold standard [32], leaving less room for measurement error.

However, this study is not without limitations. Firstly, the cross-sectional nature of the data does not allow inferences of causality. Secondly, a substantial number of participants were excluded from the analyses due to the absence of SenseWear data. A drop-out analysis confirmed our assumption that, for SenseWear data, not complying with the inclusion criteria was a random event and therefore did not influence the results (results not shown). Lastly, we could not control for medication use because data were missing, which might cause residual confounding.

In conclusion, replacing sedentary time with either sleep, LPA or MVPA was positively associated with several cardio-metabolic health risk factors. Replacing LPA with MVPA was associated only with extra benefits for clustered cardio-metabolic risk. Interventions for increasing cardio-metabolic health should focus on replacing sedentary time with either sleep, LPA or MVPA depending on the risk parameters that need to be targeted. For example, when hypertension appears to be the principal health risk, it might be sufficient to replace bouts of sedentary time with LPA, however, when the main goal is to improve clustered cardio-metabolic risk, engaging in MVPA is probably also necessary. Increasing time of substitution might lead to additional and more pronounced cardio-metabolic health benefits [10]. Further longitudinal studies investigating substitution of different types and intensities of activities of various lengths are necessary to gain better insight of the possible cardio-metabolic health benefits.

List of abbreviations

CLOCK = Circadian Locomotor Output Cycles Kaput

CMRS = Cardio-metabolic risk score

HEI = Healthy eating index

HDL-cholesterol = High Density Lipoprotein cholesterol

LPA = Light physical activity

MVPA = Moderate-to-vigorous physical activity

Declarations

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References

1. World Health Organization. Global Health Risks - Mortality and burden of disease attributable to selected major risks. Geneva: WHO; 2009.

2. Thorp AA, Owen N, Neuhaus M, Dunstan DW. Sedentary behaviors and subsequent health outcomes in adults a systematic review of longitudinal studies, 1996-2011. *Am J Prev Med*. 2011;41(2):207-215.

3. Stewart RA, Benatar J, Maddison R. Living longer by sitting less and moving more. *Curr Opin Cardiol.* 2015;30(5):551-557.

4. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc.* 2007;39(8):1423-1434.

5. Healy GN, Dunstan DW, Salmon J, et al. Breaks in sedentary time: beneficial associations with metabolic risk. *Diabetes Care*. 2008;31(4):661-666.

6. Ju SY, Choi WS. Sleep duration and metabolic syndrome in adult populations: a meta-analysis of observational studies. *Nutrition & diabetes*. 2013;3:e65.

7. Mekary RA, Willett WC, Hu FB, Ding EL. Isotemporal substitution paradigm for physical activity epidemiology and weight change. *Am J Epidemiol*. 2009;170(4):519-27.

8. Buman MP, Winkler EA, Kurka JM, et al. Reallocating time to sleep, sedentary behaviors, or active behaviors: associations with cardiovascular disease risk biomarkers, NHANES 2005-2006. *Am J Epidemiol*. 2014;179(3):323-334.

9. Hamer M, Stamatakis E, Steptoe A. Effects of substituting sedentary time with physical activity on metabolic risk. *Med Sci Sports Exerc*. 2014;46(10):1946-1950.

10. Ekblom-Bak E, Ekblom O, Bergstrom G, Borjesson M. Isotemporal substitution of sedentary time by physical activity of different intensities and bout lengths, and its associations with metabolic risk. *Eur J Prev Cardiol*. 2015;23(9):967-974.

11. Wellburn S, Ryan CG, Azevedo LB, et al. Displacing sedentary time: association with cardiovascular disease prevalence. *Med Sci Sports Exerc*. 2016;48(4):641-647.

12. Ekblom-Bak E, Ekblom O, Bolam K, Ekblom B, Bergstrom G, Borjesson M. SCAPIS pilot study: sitness, fitness and fatness - Is sedentary time substitution by physical activity equally important for everyone's markers of glucose regulation? *J Phys Act Health*. 2016;13(7):697-703.

13. Stamatakis E, Rogers K, Ding D, et al. All-cause mortality effects of replacing sedentary time with physical activity and sleeping using an isotemporal substitution model: a prospective study of 201,129 mid-aged and older adults. *Int J Behav Nutr Phys Act.* 2015;12:121.

14. Matton L, Beunen G, Duvigneaud N, et al. Methodological issues associated with longitudinal research: findings from the Leuven Longitudinal Study on Lifestyle, Fitness and Health (1969 - 2004). *J Sports Sci*. 2007;25(9):1011-1024.

15. Johannsen DL, Calabro MA, Stewart J, Franke W, Rood JC, Welk GJ. Accuracy of armband monitors for measuring daily energy expenditure in healthy adults. *Med Sci Sports Exerc*. 2010;42(11):2134-2140.

16. Bhammar DM, Sawyer BJ, Tucker WJ, Lee JM, Gaesser GA. Validity of SenseWear Armband v5.2 and v2.2 for estimating energy expenditure. *J Sports Sci*. 2016;34(19):1830-1838.

17. Shin M, Swan P, Chow CM. The validity of Actiwatch2 and SenseWear armband compared against polysomnography at different ambient temperature conditions. *Sleep Science.* 2015;8(1):9-15.

18. De Baere S, Lefevre J, De Martelaer K, Philippaerts R, Seghers J. Temporal patterns of physical activity and sedentary behavior in 10–14 year-old children on weekdays. *BMC Public Health.* 2015;15:791

19. Orme M, Wijndaele K, Sharp SJ, Westgate K, Ekelund U, Brage S. Combined influence of epoch length, cut-point and bout duration on accelerometry-derived physical activity. *Int J Behav Nutr Phys Act.* 2014;11(1):34.

20. Scheers T, Philippaerts R, Lefevre J. Variability in physical activity patterns as measured by the SenseWear Armband: how many days are needed? *Eur J Appl Physiol.* 2012;112(5):1653-1662.

21. Wijndaele K, Orrow G, Ekelund U, et al. Increasing objectively measured sedentary time increases clustered cardiometabolic risk: a 6 year analysis of the ProActive study. *Diabetologia*. 2014;57(2):305-312.

22. World Health Organization. MONICA Project Manual. Geneva: WHO, Cardiovascular Diseases Unit; 1990.

23. Guenther PM, Casavale KO, Reedy J, et al. Update of the Healthy Eating Index: HEI-2010. J *Acad Nutr Diet.* 2013;113(4):569-580.

24. Duvigneaud N, Matton L, Wijndaele K, et al. Relationship of obesity with physical activity, aerobic fitness and muscle strength in Flemish adults. *J Sports Med Phys Fitness.* 2008;48(2):201-210

25. Wientzek A, Floegel A, Knuppel S, et al. Serum metabolites related to cardiorespiratory fitness, physical activity energy expenditure, sedentary time and vigorous activity. *Int J Sport Nutr Exerc Metab*. 2014;24(2):215-226.

26. Prasai MJ, George JT, Scott EM. Molecular clocks, type 2 diabetes and cardiovascular disease. *Diabetes Vasc Dis Re*. 2008;5(2):89-95.

27. Sassen B, Cornelissen VA, Kiers H, Wittink H, Kok G, Vanhees L. Physical fitness matters more than physical activity in controlling cardiovascular disease risk factors. *Eur J Cardiovasc Prev Rehabil.* 2009;16(6):677-683.

28. He XZ, Baker DW. Differences in leisure-time, household, and work-related physical activity by race, ethnicity, and education. *J Gen Intern Med.* 2005;20(3):259-266.

29. Bouchard C. Physical activity and health: introduction to the dose-response symposium. *Med Sci Sports Exerc*. 2001;33(6 Suppl):S347-3450.

30. Bailey DP, Locke CD. Breaking up prolonged sitting with light-intensity walking improves postprandial glycemia, but breaking up sitting with standing does not. *J Sci Med Sport.* 2015;18(3):294-298.

31. Scheers T, Philippaerts R, Lefevre J. SenseWear-determined physical activity and sedentary behavior and metabolic syndrome. *Med Sci Sports Exerc*. 2013;45(3):481-489.

32. Vanhees L, Lefevre J, Philippaerts R, et al. How to assess physical activity? How to assess physical fitness? *Eur J Cardiovasc Prev Rehabil*. 2005;12(2):102-114.

Table 1. Descriptive statistics for personal characteristics, sleep & physical activity, and cardio-metabolic risk factors

	Total (*n*=410)			
Variables	***Mean***	***SD***	***Med***	***IQR***
Personal characteristics				
Age (years)	55.5	9.6	/	/
Weight (kg)	75.2	12.4	/	/
VO_2peak (ml.min^{-1}.kg^{-1})	/	/	32.0	[28.0; 38.5]
Sleep & physical activity				
Sleep (minutes/day)	389	60	/	/
Sedentary time (minutes/day)	646	110	/	/
LPA (minutes/day)	/	/	230	[186; 280]
MVPA (minutes/day)	/	/	129	[83; 204]
Cardio-metabolic markers				
Waist circumference (cm)	85.7	10.3	/	/
Fasting glucose (mmol/L)	/	/	5.06	[4.78; 5.44]
HDL-cholesterol (mmol/L)	/	/	1.47	[1.24; 1.76]
Triglycerides (mmol/L)	/	/	0.99	[0.76; 1.34]
Diastolic blood pressure (mmHg)	86	9	/	/
Systolic blood pressure (mmHg)	135	17	/	/

Note. *SD* = standard deviation, Med = median, IQR = interquartile range

LPA = Light physical activity

MVPA = Moderate-to-vigorous physical activity.

“Substituting Sedentary Time With Light And Moderate-to-Vigorous Physical Activity is Associated With Better Cardio-Metabolic Health” by Knaeps S et al.
Journal of Physical Activity & Health

Table 2. Pearson correlation coefficients for the association between sleep, sedentary time and physical activity (LPA and MVPA), and cardio-metabolic health parameters

	CMRS	Waist circumference	Fasting glucose	HDL-cholesterol	Triglycerides	Systolic blood pressure	Diastolic blood pressure
Sleep	.06	-.09	.04	.10*	.03	.05	-.03
Sedentary time	.14**	.29***	.03	-.27***	.11**	.12*	.12*
LPA	.11*	-.04	-.04	.22**	-.02	-.15**	-.09
MVPA	-.30***	-.26***	-.03	.09	-.15**	-.04	-.05

CMRS = Clustered cardio-metabolic risk, LPA = Light physical activity, MVPA = Moderate-to-vigorous physical activity.

*p<.05; **p<.01;***p<.001

Table 3. Effects and 95% confidence intervals of replacing 30 minutes of sedentary time with 30 minutes of sleep, LPA or MVPA for clustered cardio-metabolic risk and cardio-metabolic health parameters

Replace 30 minutes of sedentary time with	Sleep	LPA	MVPA
Clustered cardio-metabolic risk	0.00 (-0.00; 0.00)	0.00 (-0.00; 0.00)	**-0.06 (-0.08;-0.04)**
Waist circumference (cm)	**-0.86 (-1.33;-0.40)**	**-0.50 (-0.89;-0.11)**	**-0.95 (-1.27;-0.63)**
Fasting glucose (mmol/L)	-0.01 (-0.04; 0.02)	-0.01 (-0.04; 0.01)	0.00 (-0.02; 0.02)
HDL-cholesterol (mmol/L)	**0.03 (-0.01; 0.05)**	**0.04 (0.03; 0.06)**	**0.02 (0.01; 0.03)**
Triglycerides (mmol/L)	0.01 (-0.04; 0.02)	-0.01 (-0.04; 0.02)	**-0.04 (-0.06;-0.01)**
Systolic blood pressure (mmHg)	-0.35 (-0.81; 0.11)	**-0.41 (-0.80;-0.03)**	-0.20 (-0.52; 0.12)
Diastolic blood pressure (mmHg)	-0.44 (-1.21; 0.33)	**-1.17 (-1.81;-0.53)**	-0.17 (-0.71; 0.36)

Data are unstandardized regression coefficients

Isotemporal substitution model including all activity variables (MVPA & LPA) and sleep; additionally adjusted for total wear time, age, sex, education level, healthy eating index and smoking status

Results in bold: p<.05

LPA = Light physical activity, MVPA = Moderate-to-vigorous physical activity.

Table 4. Effects and 95% confidence intervals of replacing 30 minutes of LPA with 30 minutes of sleep, sedentary time or MVPA for clustered cardio-metabolic risk and cardio-metabolic health parameters

Replace 30 minutes of LPA with	Sleep	Sedentary Time	MVPA
Clustered cardio-metabolic risk	-0.01 (-0.05; 0.03)	-0.01 (-0.04; 0.01)	**-0.08 (-0.11;-0.04)**
Waist Circumference (cm)	-0.36 (-0.92; 0.20)	**0.50 (0.11; 0.89)**	-0.45 (-0.90; 0.00)
Fasting Glucose (mmol/L)	0.01 (-0.03; 0.04)	0.01 (-0.01; 0.04)	-0.01 (-0.01; 0.04)
HDL-cholesterol (mmol/L)	-0.01 (-0.04; 0.01)	**-0.04 (-0.06;-0.03)**	**-0.02 (-0.04;-0.00)**
Triglycerides (mmol/L)	0.02 (-0.02; 0.06)	0.01 (-0.02; 0.04)	-0.02 (-0.05; 0.01)
Systolic Blood Pressure (mmHg)	0.07 (-0.49; 0.62)	**0.41 (0.03; 0.80)**	0.21 (-0.23; 0.66)
Diastolic Blood Pressure (mmHg)	0.74 (-0.19; 1.66)	**1.17 (0.53; 1.81)**	**1.00 (0.26; 1.74)**

Data are unstandardized regression coefficients

Isotemporal substitution model including sedentary time, MVPA and sleep; additionally adjusted for total wear time, age, sex, education level, healthy eating index and smoking status

Results in bold: $p<.05$